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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/812,382	03/20/2001	Ashutosh Chilkoti	4176-101	1286

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
PO BOX 14329
RESEARCH TRIANGLE PARK, NC 27709

EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	**PAPER NUMBER**
1652	10

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/812,382	CHILKOTI, ASHUTOSH	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-75 is/are pending in the application.

4a) Of the above claim(s) 35-65 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-34 and 66-75 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6,8,9.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The response filed on September 11, 2002 as paper No. 9 is acknowledged. Amendment to the claims have been entered as requested. Claim 9 is amended; new claims 66-75 are added. Claims 1-75 are pending. The elected claims 1-34 and 66-75 are the subject of this Office Action. Claims 35-65 are withdrawn from consideration as directed to the non-elected invention.

DETAILED ACTION

1. Election

Applicant's election with traverse of Group I (claims 1-34) in Paper No. 9 is acknowledged. Newly added claims 66-75 read on the elected invention. The traversal is on the ground(s) that the examiner should "reconsider the restriction requirement with respect to all identified groups, and particularly with respect to the Group I and II claims (protein and DNA encoding the same), and with respect to Group I and Group IV claims (protein and method of purification of same, wherein all claims reside in class 530, and the search effort would not be unduly burdensome)."

Applicants' arguments have been fully considered, but they are found not persuasive for the following reasons.

Although the search of Group I and II is coextensive it is not overlapping, as indicated by different classification of Group I and II. Proteins of the instant application are classified in class 530, subclass 350, which encompasses proteins that consist of more than 100 amino acids, whereas Group II is classified in class 435 subclass 69.1 encompassing recombinant production of protein. Group II requires also searching for

transformants used for expression of DNA encoding the protein of Group I. Thus searching both groups together would involve undue burden to the Examiner.

Similarly, searching for Group I and Group IV **would** involve undue burden to the Examiner, because, although Group I and IV are classified in one class 530, the subclasses are different: 350 and 412, and collection of sequence data and patent and non patent literature on both subjects are enormous.

In conclusion, for the reasons indicated in the previous Office Action, paper no. 7, and above, the requirement is still deemed proper and is therefore made FINAL.

2. Objections

2.1. Drawings

The Draftsman's objection(s) to the drawings is enclosed here in the notice on form PTO-948.

The examiner noticed that Fig. 7 and 9 have no description of y-axes. Fig. 3 contain the name tendarristat, whereas the specification and Fig. 3 recite tendamistat. Corrections are required.

2.2. Claims

Claims 71-75 recite the "term ELP fusion protein." The abbreviation ELP should be expanded when used in the claims for the first time.

Applicant is advised that should claim 27 be found allowable, claim 29 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both

cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The

3. Rejections

3.1. 35 USC section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-7, 25, 26, 31 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, 25 and 26 being directed to a fusion protein recite the terms "biological molecules" and a "biologically active molecule." A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions

of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claim 1 recites the broadest recitation "biological molecules", the narrower recitiation "a biologically active molecule", and the claim is directed to "a fusion protein" which is the narrowest statement of the range/limitation.

For examination purposes it is assumed that the biological molecule and biologically active molecule are proteins.

Claim 1 is also rejected because it recites the phrase "a phase transition joined to the biologically active molecule." The phrase is confusing, because a phenomenon, the phase transition, cannot be joined to any molecule.

Claim 2 recites the term non-peptide proteins, which is indefinite and renders the claim indefinite. For examination purposes it is assumed that a "non-peptide protein" is a protein that is longer than 100 amino acids.

Claim 8 recites the phrase "the protein of interest" which is indefinite and renders the claim indefinite.

Claim 20 is rejected because the claim being dependent on claim 1 does not further limit the base claim.

Claim 25 is confusing. Although it is clear that the fusion protein comprising biological proteins (a), (b) and a spacer sequence (c) may be produced recombinantly, it is not clear what the Applicant mean when they say that any of the biological molecule (a), (b) and (c) may be produced recombinantly. For example, how to produce

recombinantly lipids? Also it is not clear how the parts of the fusion protein are to be produced independently and after that to be somehow joined.

Claim 26 is confusing. It is not clear what applicants mean by produced synthetically? Does "synthetic" refer to chemical structures, like amino acids and other not found in nature, i.e. man-made?

Part c) in claims 31 and 33 is directed to itself.

3.2. 35 USC section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3.2.1. Lack of written description

Claim 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to a fusion protein comprising one or more biologically active molecules, and one or more protein exhibiting a phase transition.

Applicants' invention is a fusion protein exhibiting a phase transition. Claim 1-11 are directed to large and variable genus of biologically active molecules that consist part (a) of the fusion protein, however neither the claim nor the specification set forth their structures, and neither the claims nor the specification do not particularly point out

which features of the biologically active proteins ensure the capacity of exhibiting the phase transition of the fused protein the part of which they are going to be. The specification teaches two species of the genus, thioredoxin and tendamistat. This is not enough for identifying the features of all biologically active molecules, natural and man-made. More important, all biologically active molecules are unable to support the capacity of exhibiting the phase transition.

Taking into account lack of written description of structures of molecules of the claimed genus the examiner concludes that the inventors were not in possession of the claimed invention at the time the application was filed.

Claims 2-3 and 5-7 are rejected because the claims are directed to large and variable genera of:

(a) lipids and carbohydrates;

(b) peptides;

(c) therapeutic proteins

(d) enzymes useful in industrial biocatalysis;

(e) antibodies and antibodies fragments

that are not described by structure and function by Applicants. All molecules of the genera claimed by claims 2-3 and 5-7 are unable to support the desired capacity of exhibiting the phase transition of the fused protein the part of which they are going to be see the above rejections of claim 1-11.

The one skilled in the art concludes that the inventors were not in possession of the claimed invention at the time the application was filed.

Claim 11, 29 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is directed to a large and variable genus of proteins exhibiting a ß-turn said proteins being contained in the claimed invention. The specification provides exemplary subgenus of the claimed genus consisting of pentapeptide Val-Pro-Gly-X-Gly, however, the specification does not teach the structure of all possible proteins exhibiting a ß-turn. Therefore, the one skilled in the art concludes that the inventors were not in possession of the claimed invention at the time the application was filed.

Claim 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a large and variable genus signal peptides that are comprised in the fusion protein exhibiting phase transition. However, the specification is silent about the structure of a fusion protein containing any signal peptide. Therefore, the one skilled in the art concludes that the inventors were not in possession of the claimed invention at the time the application was filed.

Claim 26 is rejected because Applicants do not disclose any protein consisting of parts (a), (b), and (c) that were produced synthetically.

3.2.2. Scope of enablement

Claim 1-34, and 66-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fusion protein exhibiting a phase transition and comprising

(a) tioredoxin and/or tendamistat,

(b) pentapeptide Val-Pro-Gly-X-Gly, in one or many copies, and

(c) a spacer cleavable by thrombin

does not reasonably provide enablement for any ELP fusion protein and specifically does not provide enablement for any molecule consisting of parts (a), (b), (c) when

part (a) is:

any biologic molecule,

any peptide, any lipid, and carbohydrate,

any biologically active protein,

any therapeutic protein,

any industrial biocatalyst,

any antibody or its fragment,

any protein of interest,

comprising any signal peptide,

wherein the above molecules are natural or man-made;

part (b) is:

any protein exhibiting a phase transition joined to any biologically active protein,

comprising protein exhibiting a ß-turn,

consisting of the oligomeric repeats wherein the ratio of Val-Pro-Gly-X-Gly, to other amino acid residues of the ELP is greater than 75%,

any ELP,

wherein the above molecules are natural or man-made

part (c) is :

any spacer, and

a spacer comprising any proteolytic cleavage site.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the

nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any fusion protein comprising any elastin-like peptides, single or in many copies, wherein said elastin-like peptides are listed under part (b) above; one or more other proteins listed under part (a) above, but also molecules other than proteins; and a spacer as defined under part (c) above. Although the knowledge of production of fusion protein is well developed and skills of artisans highly developed it is not possible for any person skilled in the art to make invention commensurate with the scope of claims 1-34 and 66-75. In addition, it is not only that one has to make a fusion protein, but **more important, this fusion protein has to exhibit the phase transition phenomenon.** Therefore any fusion protein constructed as described by claims 1-34 and 66-75 has to be check for the capacity of phase transition. Thus, the experimentation necessary to make the invention is out of the realm of routine experimentation.

The specification provides chemical structure and other identifying characteristics, as well as describes recombinant production of a fusion protein consisting of

(a) tioredoxin and/or tendamistat,

(b) pentapeptide Val-Pro-Gly-X-Gly, in one or many copies, and

(c) a spacer cleavable by thrombin.

The specification is not enabling for extremely large scope of molecules that may be components of the fused molecules of claimed invention. The genera of molecules called (a), (b) and (c) above are not sufficiently described, as to their structure; see rejection for lack of written description. Without further guidance on the part of Applicants regarding the structure that ensures the desired characteristic of the fusion proteins, i.e., the capacity of phase transition, the probability of success in making the claimed invention is low, and experimentation left to those skilled in the art improperly extensive and undue.

3.3. 35 USC, section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 71 is rejected under 35 U.S.C. 102(b) as being anticipated by McPherson et al. (Production and Purification of a Recombinant Elastomeric Polypeptide, G-$(VPGVG)_{19}$-VPGV, from *Escherichia coli*, Biotechnol. Prog. (1992), 8, 347-352, enclosed in Information Disclosure Statement).

McPherson et al. teach a fusion protein consisting of glutathion S-transferase joined trough glycine spacer to the pentapeptide $(VPGVG)_{10}$ or to $(VPGVG)_{19}$ – VPGV. The glycine spacer creates the protease recognition site for protease factor Xa (page 347, abstract, and the right column above "Materials and Methods"). The protein

disclosed by McPherson consists of a fusion of glutathion S-transferase and the repeating peptides of elastin (see page 34, left column, line 5).

Claim 71 of the present application is directed to an ELP fusion protein. According to the specification, page 2, line 4 and 10, elastin-like peptide (EPL) is the pentapeptide Val-Pro-Gly-X-Gly, when X is any amino acid, including V. Thus, the subject mater and the scope of claim 71 is the one of the fusion protein taught by McPherson et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600